

Applicants: David J. Pinsky, et al.  
Serial No.: 10/692,439  
Filed: October 22, 2003  
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#### REMARKS

Claims 25 is pending in the subject application. Applicants have not added, canceled or amended any claims. Therefore, claim 25 is still pending and under examination.

#### Withdrawal of Rejections under 35 U.S.C. §112, First Paragraph

Applicants acknowledge the Examiner's withdrawal of the previous rejections of claim 25 under 35 U.S.C. §112, first paragraph, as set forth on page 2 of the August 7, 2007 Final Office Action.

#### Obviation of Rejection under 35 U.S.C. 103(a)

Applicants acknowledge the Examiner's indication that the rejection of claim 25 under 35 U.S.C. §103(a) as being unpatentable over Toledo-Pereyra in view of Benedict, et al. and King has been obviated, as set forth on page 3 of the August 7, 2007 Final Office Action.

#### Withdrawal of Rejection on the Ground of Nontatutory Obviousness-Type Double Patenting

Applicants acknowledge the Examiner's withdrawal of the rejection of claim 25 on the ground of nonstatutory obviousness-type double patenting over claims 1-19 of U.S. Patent No. 6,316,403 in view of Toledo-Pereyra and King, as set forth on page 3 of the August 7, 2007 Final Office Action.

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**Rejection under 35 U.S.C. 103(a)**

The Examiner rejected claim 25 under 35 U.S.C. 103(a) as allegedly obvious over Toledo-Pereya, in view of Benedict, et al. and the product use sheet for 1,5-dansyl-Glu-Gly-Arg chloromethyl ketone from Calbiochem ("the product use sheet").

Specifically, the Examiner alleged that Toledo-Pereya teaches that fibrinogen activation and clotting (i.e. thrombosis) is a pathophysiological event in reperfusion injury that needs to be treated with pharmacological agents to inhibit coagulation. However, the Examiner indicated on page 5 of the Office Action that Toledo-Pereya fails to teach the administration of Factor IXa compounds to treat thrombosis in reperfusion injury.

To cure this deficiency of Toledo-Pereya, the Examiner cited Benedict, et al. and the product use sheet for 1,5-dansyl-Glu-Gly-Arg chloromethyl ketone from Calbiochem. The Examiner alleged that Benedict, et al. teach that inactivated Factor IXa was successful for inhibiting thrombus formation *in vivo*. The Examiner further indicated that Benedict, et al. teach making inhibited Factor IXa by incubating Factor IXa with Glu-Gly-Arg-chloromethyl ketone, but not by incubating Factor IXa with 1,5-dansyl-Glu-Gly-Arg-chloromethyl ketone. However, the Examiner alleged that the product use sheet teaches that the use of a fluorophore (i.e. dansyl) on the enzyme inhibitor allows for direct monitoring of interactions of the labeled enzyme/inhibitor complex, and that one skilled in the art would have been motivated to substitute the Glu-Gly-Arg-chloromethyl ketone taught by Benedict, et al. with the 1,5-dansyl-Glu-Gly-Arg-chloromethyl ketone taught by the product

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use sheet.

Therefore, the Examiner alleged that it would have been obvious to a person skilled in the art at the time the invention was made to administer Factor IXa inactivated by 1,5-dansyl-Glu-Gly-Arg-chloromethyl ketone to patients to treat reperfusion injury.

In response to the Examiner's rejection, applicants respectfully traverse.

In order for a claimed invention to be obvious over the cited references, the cited references, when combined, must teach or suggest each element of the invention. Applicants maintain that the cited references fail to do this.

Specifically, applicants maintain that nowhere do the cited references teach or suggest the use of 1,5-dansyl-Glu-Gly-Arg-chloromethyl ketone to inactivate Factor IXa, as recited in pending claim 25. The Examiner cited the product use sheet for 1,5-dansyl-Glu-Gly-Arg-chloromethyl ketone, alleging that based on its teaching, one skilled in the art would find it obvious to substitute the Glu-Gly-Arg-chloromethyl ketone taught by Benedict, et al. to inactivate Factor IXa with 1,5-dansyl-Glu-Gly-Arg-chloromethyl ketone. However, applicants note that the product use sheet merely teaches the use of 1,5-dansyl-Glu-Gly-Arg-chloromethyl ketone to inhibit Factor Xa. Nowhere does the product use sheet teach or suggest that 1,5-dansyl-Glu-Gly-Arg-chloromethyl ketone would be effective in inactivating Factor IXa. Accordingly, applicants maintain that the cited references, when combined, do not teach or suggest each element of the claimed invention and

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therefore, claim 25 is not obvious over Toledo-Pereya, in view of Benedict, et al. and the product use sheet.

In view of the preceding remarks, applicants respectfully request that the Examiner reconsider and withdraw the rejection of claim 25 under 35 U.S.C. §103(a).

#### **Summary**

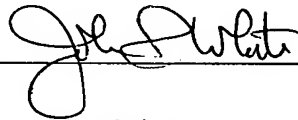
In view of the preceding remarks, applicants maintain that pending claim 25 is in condition for allowance, and respectfully request that the Examiner issue a notice of allowance.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invite the Examiner to telephone him at the number provided below.

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No fee is deemed necessary in connection with the filing of this Communication. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

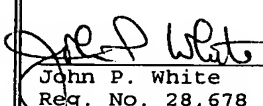
Respectfully submitted,



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